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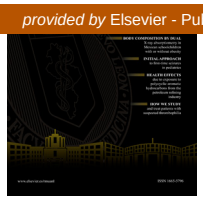

EDITORIAL

Changing the rules of engagement: Perspective of Zika virus

Those of you that have been in the medical field for some years might recall that over the last 3 decades, we have encountered outbreaks and epidemics caused by old enemies that for some reason reemerged. These ''upgraded'' microorganisms reappeared because of genetic re-engineering and/or human error; some examples include (but are not restricted to) AH1N1 influenza, Ebola, MERS, measles, cholera, etc. These epidemiological events as others cause morbidity in high risk groups that in most cases include pregnancy and children. But in the last 50 years no infectious agent of epidemic proportions has been directly linked to birth defects and fetal death; Thus the rules of engagement change.

Zika virus (ZIKV) is not new, description of the virus dates back to 1952, what is new is our understanding of its effects and the widespread dissemination. There is now robust evidence of its causal effect on fetal deaths, microcephaly, in utero growth restriction, ventricular calcifications, central nervous system abnormalities, and changes in amniotic fluid volume as well as cerebral and umbilical artery flow. Furthermore, association between ZIKV infection and Guillain–Barre syndrome are growing.[1]

The rapid spread of the virus is another key factor. Like other arbovirus, ZIKV uses a common mosquito (*Aedes* spp.) for transmission and has spread exponentially in *Aedes* endemic regions. Since 2007, 62 countries and territories have documented cases, 33 of those are from the region of the Americas since 2015. More than 1000 cases of microcephaly have been reported from 8 countries an another 13 have reported an increase incidence in GBS linked to ZIKV.[2] Recent knowledge of other mechanisms of transmission other than mosquito bites such as sexual intercourse,[3] blood donations and persistence of RNA in body fluids[4] brings new insight to the understanding of physiopathology.

The disease is fairly mild in most cases and has an extremely low mortality rate in the immunocompetent non-pregnant adult; with symptomatic treatment the recovery rate is excellent. The caveat is that this is completely different in the pregnant patient. Approximately 80% of infected patients will not develop symptoms and about 40–50% of pregnant woman infected with ZIKV will do so.[5] To that the diagnostic capability is poor, the methods exist but they are not readily available in highly prevalent areas. Detection by PCR is performed in reference laboratory's but samples are mainly drawn from symptomatic patients and since the current PCR assay detects viral RNA, it only will be positive during the period of viremia (5–7 days), which may be relatively short thus underestimating the incidence. Antibody testing has to be confirmed by elevation of titers or a molecular method and there is the problem of cross-reactivity between flaviviruses. IgM-antibody assays cannot reliably distinguish between ZIKV and dengue virus (DENV) infections. Therefore, an IgM-positive result on an enzyme-linked immunosorbent assay for DENV or Zika IgM should be considered indicative of a recent flavivirus infection. The same is true for patients that who have received yellow fever or Japanese encephalitis vaccine or have previously been infected with another flavivirus, cross-reactive antibodies may make it difficult to determine which flavivirus is causing the current illness. But let's idealize that these methods are available and accessible... What do we tell the pregnant patient after the test comes back positive? Anything we can say other than ''everything will be all right'' to this point is unsettling for a mother to be, and unfortunately we cannot assure a good outcome.

The World Health Organization recently declared ZIKV a global emergency, this gives the highest priority for epidemiological control efforts; among other things it opens up grants for research and expedites approval of research protocols. Treatment for these types of viruses such as DENV, Chikungunya, etc. are cumbersome to develop more over the diseases they cause is self limited. Vector control measures are inconsistent, especially in underdeveloped countries and are subject to many environmental, social and even political variables; this makes vaccine development the obvious choice. The technological tools exist and make a vaccine feasible, although animal models and preclinical trials will have to be expedited. A major advance in developing the counterattack is that Brazil's Agência Nacional de Vigilância Sanitária, the U.S. Food and Drug Administration, and

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the European Medicines Agency have committed to prioritizing the expedited evaluation of Zika products. Also, there is a real-time posting of preliminary information regulated by the International Committee of Medical Journal Editors clarifying that prepublication dissemination of critical information will not prejudice later journal publication related to ZIKV or future public health emergencies has been helpful these advances are unprecedented and will surely lead to vaccine development. Although some questions start to come up, after the preclinical trials who will be the first targeted population to receive the vaccine? Nonpregnant adult women? Pregnant patients in high risk areas? These questions are going to have to be addressed relatively quickly.

Every biological species try to preserve their young, parents will literally give their lives for their offspring in order to continue the species' existence; Humans do not differ. We as a species, have done extraordinary things to preserve our next generations, we develop vaccines, medications, programs for food and clean water access, etc. We may be tolerable to some extent to other illness, but not those that compromise our unborn children and their pregnant mothers, here there is no tolerance. Many questions remain unanswered for now, but what is clear is that in order to control and prevent the spread of ZIKV we must change the way we commonly think for this old fowl is not a common one.

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